REMARKS

Summary of the Invention

The invention relates to a method of identifying patients to receive cholinomimetic drugs as treatment for neurological disease. Patients that are to receive cholinomimetic therapy are identified by determining the number of copies of apoE4 gene alleles.

Summary of the Office Action

Claims 1-8 are pending. Claims 1-5 and 8 stand rejected under 35 U.S.C. § 112, second paragraph, and under the judicially created doctrine of obviousness-type double patenting. Each of these issues is addressed below.

Support for the Amendments

Claims 1, 4, and 5 have been amended to replace "the number of copies" with "presence." The support for these amendments are found on page 6, line 9; pages 7, lines 23- 35; page 8, lines 1-15; page 12, lines 3-5; and Figures 1, 4, and 6. Claim 1 has been amended to replace "respond to" with "receive beneficial effects." The support for this amendment are found on pages 13, line 27, to page 15, line 13-24; page 16, lines 13-24; and Figure 8. Claim 4 has been amended to replace "subgroup" with "group that either receives or does not receive said drug." The support for this amendment are found on page 2, lines 22-25; page 2, line 26, to page 3, line 5; page 15, lines 5-12; page 27, lines 14-27; and page 28, lines 9-17. No new matter is added by these amendments.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-5 and 8 are rejected for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Specifically, Examiner asserts that a) claims 1, 4, and 5 do not set forth the steps in "determining the number of copies of *apoE4* gene alleles in said subject", b) claim 1 does not adequately define "respond" in the phrase "respond to a cholinomimetic drug", and c) claim 4(b) does not adequately define the term "subgroup."

To overcome Examiner's rejection, Applicant amended claims 1, 4, and 5 to distinctly claim a method comprising determining the presence of *apoE4* gene alleles. Applicant reiterates that the description of a polymerase chain reaction that can be used to determine the presence of *apoE4* alleles. The support for this amendment are found on page 6, line 9; pages 7, lines 23- 35; page 8, lines 1-15; page 12, lines 3-5; and Figures 1, 4, and 6). Accordingly, additional instruction as to determine the presence of *apoE4* alleles is not required for enablement of the present invention.

Regarding the term "respond" in the phrase "respond to a cholinomimetic drug" of claim 1, Applicant has amended this claim to more clearly define that the invention is directed to beneficial effects of cholinomimetic drugs. The support for this amendment are found on pages 13, line 27, to page 15, line 28; page 16, lines 13-24; and Figure 8. As the discussion on these pages in the specification indicate, the beneficial effects of cholinomimetic drugs take many forms including affecting cholinergic function, prevalence of AD-associated pathologies, such as, plaque and tangle formation, and time of onset of AD symptoms.

Regarding the term "subgroup" in claim 4, Applicant has amended the claim to more clearly define that the absence of *apoE4* allele in a patient will be used in determining whether or not the patient will receive the drug being tested in the clinical trial. The support for this amendment are found on page 2, lines 22-25; page 2, line 26, to page 3, line 5; page 15, lines 5-12; page 27, lines 14-27; and page 28, lines 9-17.

Rejection under doctrine of obviousness-type double patenting

Claims 1-5 and 8 are rejected as being unpatentable over claims 1-4 of U.S. Patent No. 5,935,781 ('781 patent). Specifically, Examiner asserts that the method of treating cognitive impairment in claim 1 of the '781 patent is not patentably distinct from the method of treating Alzheimer's disease in claim 1 of the application. To overcome this rejection, Applicant will submit a terminal disclaimer in compliance with 37 C.F.R. 1.321(c) once notice of otherwise allowable subject matter is received.

Conclusion

Applicant submits that the claims are in condition for allowance and such action is respectfully requested.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Washington, DC 20231

MARKED-UP VERSION OF CLAIM AMENDMENTS

1. A method for the identification of human subjects to be responsive to a cholinomimetic drug, said subjects having Alzheimer's disease, said method comprising determining the [number of copies] presence of *apoE4* gene alleles in said subject, wherein the absence of *apoE4* gene allele in a biological sample of said subject indicates a predisposition to [respond to] receive beneficial effects from a cholinomimetic drug.

4. A method for identifying a patient sample in a clinical trial of a drug for the treatment of cognitive impairments, said method comprising:

(a) identifying a patient already diagnosed with said cognitive impairments, or as being predisposed to acquire or to be at risk for said cognitive impairments; and

(b) determining the [number of copies] presence of *apoE4* gene alleles in said patient, wherein an absence of *apoE4* allele places the patient into a [subgroup] group that either receives or does not receive said drug for said clinical trial of said drug.

5. A method for identifying a patient sample in a clinical trial of a drug for the treatment of Alzheimer's disease, said method comprising:

(a) identifying a patient already diagnosed with said disease or as being predisposed to acquire or to be at risk for said disease; and

(b) determining the [number of copies] presence of *apoE4* gene alleles in said patient, wherein an absence of *apoE4* allele places the patient into a [subgroup] group that either receives or does not receive said drug for said clinical trial for the treatment of said Alzheimer's disease.